## REMARKS

In response to the above Office Action and the rejection of the claims under §112, second paragraph, claims 1 and 2 have been amended to make it clear that it is the claimed thiazole compound or a salt thereof that is the active ingredient in the enema preparation and that it is one tenth as much as the amount used with oral administration. Conforming amendments have also been made to claims 8, 10, 12, and 13.

It is believed this should also take care of the rejection of the claims for obviousness-type double patenting over copending Application No. 10/424,904.

In the Office Action, the Examiner rejected claims 1-7 under 35 U.S.C. §102(b) for being anticipated by the article to Banan et al., hereafter Banan. Claims 1, 4, and 8-13 were also rejected under 35 U.S.C. §103(a) for being obvious over Chihiro in view of Remington's Pharmaceutical Sciences, hereafter Remington's.

In Banan, it is described that though the most suitable administrating route of an OPC compound, which is an active ingredient of the present invention, is considered to be a combined administration of system administration (oral) and topical administration (enema), the effective scavenge of the reactive oxidants produced at the basolateral or apical side of epithelial cell monolayer is possible by either the system administration (oral) or the topical administration (enema). However, it is also disclosed in Banan that the suitable administration route should be investigated depending on the patient.

What is not disclosed or suggested in Banan is that an enema administration of the compound of the present invention requires only one tenth as much as the amount used with oral administration in order to obtain a significant inhibiting effect of the

disorder. Therefore, a remarkable decrease in the amount of the active ingredient used is possible and this results in a drastic reduction in undesirable side effects.

When mesalazine, prednisolone, methylprednisolone, dexamethasone, betamethasone and hydrocortisone known as active ingredients of marketed drugs for treating regional or ulcerative colitis are administered in the form of an enema preparation, their therapeutic effects are only improved about 1.2 to 2.3 times as compared to administration in the form of an oral or injection preparation.

From the above discussion, one skilled in the art would not easily, therefore, expect that an enema administration of the compound of the present application would require only one tenth as much as the amount used with an oral administration in order to obtain a significant inhibiting effect of the disorder.

Accordingly, it is submitted the claims cannot be considered to be anticipated by Banan.

With respect to the rejection of the claims under §103(a), Applicants provide the following information.

The dose regimen and dosages for commercially available oral and enema preparations for inflammatory bowel diseases are summarized in the Table below. This data is based on information from the reference "2005 DRUGS IN JAPAN ETHICAL DRUGS."

| Drug | Oral dosage | Enema dosage | Oral/EnemaDosage Ratio |
|---|---|---|---|
| Mesalazine | 1.5-2.25 g/day | 1 g/time | 2.25 |
| Prednisolone | 5-60 mg/day (as prednisolone moiety) | 2-30 mg/time (as prednisolone moiety) | 2 |
| Dexamethasone | 0.5-8 mg/day (as dexamethasone moiety) | 0.4-6 mg/time | 1.3 |
| Betamethasone | 0.5-8 mg/day | 1.5-6 mg/time | 1.3 |
| Hydrocortisone | 10-120 mg/day | 50-100 mg/time | 1.2 |
| Methylprednisolone | 4-48 mg/day | 40-120 mg/time | 0.4 |

The original specification demonstrates through pharmacological data on pages 10 to 13, particularly on page 12, line 20 to page 13, line 4 that when a compound according to the present invention is administered in the form of an enema preparation, the dosage can be lowered to one-tenth and still significantly exhibit a disorder suppressing effect compared to when it is orally administered. Thus the amount of the drug used can be remarkably reduced, resulting in a drastic suppression of adverse side effects (see page 8, line 27 to page 9, line 6 of the specification). The present invention is made based on this finding.

As shown in the above Table, when a drug is administered in the form of an enema preparation, a relatively high therapeutic effect can generally be expected because the active ingredient can directly reach an affected area in need of treatment. However, even if commercially available drugs for treating regional enteritis or ulcerative colitis, such as mesalazine, prednisolone, dexamethasone, betamethasone, hydrocortisone and methylprednisolone, are administered in the form of an enema preparation, their therapeutic effects are only improved about 1.2 to 2.3 times compared to administration in the form of an oral or injection preparation (see page 2, line 25 to page 3, line 6 of the specification).

In the present invention the amount of the active ingredient used in the preparation can be significantly reduced by changing it to the form of an enema preparation and to an extent that it could not have been expected one could do so from commercially available drugs.

This is not described or suggested in Chihiro, in view of Remington. Because the present invention according to the above amended claims achieves such an

unexpectedly and remarkable improvement in efficacy, it cannot be considered to be obvious in view of them.

Withdrawal of the rejection of the claims for being obvious over Chichiro in view of Remington's is, therefore, also requested.

It is believed claims 1, 4, and 8-13 are in condition for allowance.

A Request for Continued Examination is being filed with this Reply to enable the Examiner to consider the amended claims at this time.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account 06-0916.

Respectfully submitted,

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